Editorial: is thalidomide a good option for patients with refractory Crohn's disease?

Rogler, G

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Is thalidomide a good option for patients with refractory Crohn's disease?

Gerhard Rogler[1]

[1]Department of Gastroenterology & Hepatology, University Hospital of Zürich, Zürich, Switzerland

The history of thalidomide is inevitably connected with its serious teratogenicity. In recent years, however, its beneficial biological activities lead to a renaissance of its use [1]. Thalidomide has an inhibitory activity against tumor necrosis factor-α (TNF-α) known to play an important pathophysiological role in Crohn's disease (CD). In 1998 the FDA re-approved thalidomide for erythema nodosum leprosum (ENL) and recently for multiple myeloma [2].

As thalidomide targets TNF and there are refractory CD patients in need for additional treatments thalidomide has been introduced in CD treatment and several reports have been published recently[3-6]. Gerich and colleagues report on the outcome of 37 patients with refractory CD from a single-centre, retrospective, observational cohort from the Cedars-Sinai Medical Center[7]. The patients had moderate-to-severe CD that was refractory to available standard therapies[7]. Thalidomide was administrated at a starting dose of 50–100mg at night and increased to a maximum of 200mg/day if necessary[7]. A clinical response was observed in 54% and a clinical remission in 19% of patients.

Given the risk of teratogenicity and the high rates of side effects these numbers are somewhat disappointing. They indicate that in each case a careful risk/benefit analysis will be necessary. In this real life open label setting remission rates are surprisingly lower as compared to a recent RCT in pediatric patients in whom a remission rate of 46% (12% for placebo) was reported[8]. During a median treatment time of 4.4 months adverse events occurred in 68% of patients and 38% experienced neuropathy[7]. The latter is quite a concerning number given the relatively short treatment time. This leads to an important consideration: Long term treatment at least in adult patients is not possible due to side effects[9]. So the question arises what long term benefit the treated patients can expect. Thalidomide cannot be used as maintenance therapy based on

recent reports[3-6] and the present one[9]. So is this a desirable perspective for patients that have chronic active CD and would require a maintenance treatment? Will patients want a treatment with a remission rate of 19% without a perspective of long term treatment? This remains questionable.

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